97. A kit for screening of modulators of TL-γ, comprising;

(a) a container containing biologically active TL-γ; and

(ii) instructions for assaying TL-γ activity.

98. The kit of Claim 97, wherein said TL-γ activity assay is selected from the group consisting of plus end-directed microtubule motor activity assays, binding activity assays, and ATPase activity assays.

99. The kit of Claim 97, wherein said biologically active TL-γ has identity to a TL-γ derived from *Thermomyces lanuginosus.*

100. The kit of Claim 97, wherein said biologically active TL-γ comprises a motor domain that has identity to the motor domain of *Thermomyces lanuginosus* TL-γ.

101. The kit of Claim 97, wherein said biologically active TL-γ is recombinant.

REMARKS

Claims 1-58 were originally filed in the present case. In a Restriction Requirement dated June 19, 3000, the Examiner restricted the Claims into eight Groups. In a Response dated July 19, 2000, Applicants elected the Claims in Group V (Claims 34-46), with traverse and cancelled the Claims in the remaining Groups without prejudice.

In the present Office Action, the Examiner has set forth various rejections, as indicated below:

1) Claims 34-46 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite;

2) Claims 34, 36-39 and 41 stand rejected under 35 U.S.C. §102(a), as being allegedly anticipated by Au-Young (WO 97/43413, 11/20/97);

3) Claims 34-41 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Au-Young (WO 97/43413, 11/20/97), and Foulkes *et al.* (U.S. Patent No. 5,580,722, 12/3/96); and

4) Claims 34-39, 41, and 43-46 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Au-Young (WO 97/43413, 11/20/97).

1) THE CLAIMS ARE DEFINITE

The Examiner has rejected Claims 34-46 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Applicants must respectfully disagree. Applicants do appreciatively note that the Examiner indicates Claim 42 would be allowable if rewritten to overcome this rejection.

The Examiner indicates that Claims 34-46 are indefinite for the use of the abbreviation TL-γ in Claims 34 and 44 without indication of the meaning of the abbreviation. The Examiner also argues that there is insufficient antecedent basis for the limitation "the protein's activity" in Claim 34. In addition, the Examiner argues that Claim 34 is further indefinite for using the term "control concentration." The Examiner further argues that Claims 35-42 and 44-46 are indefinite for using the terms "A method" in Claims 35-42, and "A kit" in Claims 44-46, respectively. The Examiner also argues that Claim 35 is indefinite for using the term "the step of isolating biologically active TL-γ from a cell sample," in that it is allegedly unclear how the step of isolating fits into a method of screening modulators of TL-γ, as it "appears from claim 34 that the TL-γ is already isolated." (Office Action, page 4).

The Examiner also indicates that Claims 34-42 are indefinite for the lack of defined specific sequence for the claimed protein or a TL-γ tail domain. The Examiner argues that without reciting a specific protein sequence, one of ordinary skill in the art cannot compare two proteins using a sequence comparison algorithm. In addition, the Examiner argues that Claims 38 and 44 are indefinite for use of the term "derived,"; Claim 39 is indefinite for use of the term "small molecules,"; and Claim 42 is indefinite for using the term "TL-γ motor domain of SEQ ID NO:1." Applicants must respectfully disagree.

Nonetheless, in order to further their business interests and the prosecution of the present application, yet without acquiescing to the Examiner's rejections, and while reserving the right to prosecute the originally filed (and/or similar) Claims in the future, Applicants have cancelled Claims 34-46 without prejudice, and have added new Claims 59-101. Claims 47-68 and Claims 97-101 correspond to the cancelled Claims as originally filed. New Claims 60-96 recite additional elements that are disclosed in the Specification as filed (*See e.g.*, page 5, line 21 through page 6, line 4; page 6, line 20 through page 7, line 8; page 8, lines 13

through page 10, line 13, in particular lines 29-30 of page 9). No new matter is added in these new Claims.

Applicants submit that the use of "TL-γ" in the newly added Claims is proper, as it is the *name* (*i.e.,* it is the proper name) of the protein assigned by the inventors, and is not an abbreviation, as assumed by the Examiner. As indicated on page 23, lines 10-19, the definition of "TL-γ" indicates that TL-γ is "a plus end-directed microtubule motor protein found in hyphal fungi, which is a member of the kinesin superfamily of microtubule motor proteins and a member of the unc-104 family of motor proteins . . . ." Thus, as "TL-γ" in the Claims refers to a particular protein entity and is not an abbreviation, Applicants submit that this designation is proper.

Claim 65, which corresponds to originally filed Claim 39 recites that the candidate agent is selected from the group consisting of antibodies, proteins, oligonucleotides, nucleic acids, peptides, saccharides, fatty acids, steroids, purines, and pyrimidines. Support for this Claim is found throughout the Specification, (*See e.g.,* page 44, line 1, through page 47, line 11). In view of the newly added Claims, Applicants submit that the Claims are definite and respectfully request that this rejection be withdrawn.

2) THE CLAIMS ARE NOVEL

Claims 34-41 stand rejected under 35 U.S.C. §102(a) as being unpatentable over Au-Young (WO 97/43413, 11/20/97). On page 5 of the pending Office Action, the Examiner argues that "Au-Young teaches a method for screening therapeutic compounds/modulators which interact with/modulate a biologically active PAC10 protein . . ." The Examiner further indicates that the "PAC10 protein is a heavy chain of the kinesin family." The Examiner then argues that "[t]herefore, the PAC10 protein of Au-Young is a protein with a plus end-directed microtubule motor and a tail domain, a TL-γ protein, which has 100% identity to the motor domain of Thermomyces lanuginosus TL-γ and has identity to a TL-γ derived from Thermomyces lanuginosus. Au-Young also teaches that the biologically active PAC10 protein is recombinant and isolate from a cell sample. Thus, Au-Young meet the [sic] all limitations of the claims." (Office Action, page 5-6). Applicants must respectfully disagree.

As repeatedly indicated by the courts, anticipation requires that all of the elements and limitations of the claim be found within a single prior art reference. There must be no difference between the claimed invention and the disclosure provided by the reference, as

viewed by a person of ordinary skill in the field of the invention. (*Scripps Clinic & Research Fdtn. v. Genentech, Inc.*, 927 F.2d 1565, 1576 [Fed. Cir. 1991]). Furthermore, "[t]o establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. (*In re Royka*, 490 F.2d 981, 180 USPQ 580 [CCPA 1974]). Applicants submit that Au-Young *et al.* do not teach every element of the Claims; therefore, Au-Young *et al.* is not a proper 102 reference.

Contrary to the Examiner's assertions, Au-Young *et al.* do *not* disclose TL-γ proteins nor methods of screening for modulators of these proteins nor even kinesins. Indeed, as discussed in the Declaration of Dr. Roman Sakowicz ("Sakowicz Declaration," attached hereto at Tab A), submitted herewith, there is strong evidence that the PAC10 protein of Au-Young *et al.* does not even have the motor domain nor functions of TL-γ and other kinesin motor proteins. As stated by Dr. Sakowicz (*See,* Sakowicz Declaration, at paragraphs 6-7), and shown by the BLAST searches attached at Tab 1 to his Declaration, there is no homology between the PAC10 protein and the TL-γ protein of the presently claimed invention. Furthermore, the functions of PAC10 are not those of kinesins such as TL-γ (*See,* Sakowicz Declaration, at paragraphs 8-10. Indeed, as indicated by Dr. Sakowicz (*See,* Sackowicz Declaration at paragraph 6) and as known in the art (*See e.g.,* Hirokawa, Scinece 279:519-529 [1998], attached hereto at Tab B), the kinesin motor domain is a defining signature of kinesin family members. As there is no motor domain associated with PAC10 of Au-Young *et al.,* the TL-γ of the presently claimed invention and PAC10 of Au-Young *et al.* are clearly different proteins. Thus, contrary to the Examiner's assertions, there is no teaching in the art (nor Au-Young *et al.*) that the PAC10 of Au-Young is the same as TL-γ. Indeed, there is strong scientific evidence, as indicated in the Sakowicz Declaration and supporting materials, that the proteins of Au-Young *et al.* and the presently claimed invention are very different. As the elements of Au-Young *et al.* are *not* the same as those presently claimed, Applicants submit that Au-Young *et al.* do not anticipate the pending Claims and respectfully request that this rejection be withdrawn.

3) THE CLAIMS ARE UNOBVIOUS

The Examiner has rejected Claims 34-41 under 35 U.S.C. §103(a) as allegedly being unpatentable over Au-Young (as above) and Foulkes *et al.* (U.S. Patent No. 5,580,722, 12/3/96). The Examiner has also rejected Claims 34-39, 41, and 43-46 under 35 U.S.C.

§103(a) as allegedly being unpatentable over Au-Young. As the newly added Claims correspond to these rejected Claims, Applicants address the Examiner's rejections as applied to the newly added Claims.

A. **The Claims are Unobvious Over Au-Young *et al.* and Foulkes *et al.***

The Examiner argues that it would have been obvious to "combine the screening method for modulators of TL-γ of Au-Young and the high-throughput screen technique of Foulkes et al because the known benefit of the high-throughput screen can be sued to determine whether or not a molecule can be a modulator of protein biosynthesis and is capable of directly and specifically transcriptionally modulating the expression of a gene encoding a protein of interest." (Office Action, pages 6-7). Applicants must respectfully disagree. In addition, Applicants note that the Examiner admits that the Au-Young *et al.* reference "does not expressly teach that the screening occurs in a multi-well plate as part of a high-throughput screen." (Office Action, page 6). Applicants submit that such teachings are likewise not provided by Foulkes *et al.,* as presently claimed.

Applicants assert that the Examiner has not established *prima facie* obviousness. A *prima facie* case of obviousness requires the Examiner to cite to a reference which (a) discloses all the elements of the claimed invention, (b) suggests or motivates one of skill in the art to combine or modify those elements to yield the claimed combination, and (c) provides a reasonable expectation of success should the claimed combination be carried out (*See, e.g., Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990); and *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988)). Failure to establish **any one** of these three requirements precludes a finding of a *prima facie* case and, without more, entitles Applicant to allowance of the claims at issue. As stated in *In re Dow Chemical Co.*, 5 USPQ2d 1529 (Fed. Cir., 1988):

> The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art . . . . Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure.

Applicants assert that neither of the cited references, alone or in combination, teach the presently claimed screening methods. As discussed above, the primary reference Au-Young *et al.,* does **not** teach the presently claimed invention. The Examiner has attempted to remedy the deficiencies of Au-Young *et al.* by combining this reference with Foulkes *et al.* However, Applicants submit that neither of these references, taken alone, or in combination, teach the presently claimed invention. Thus, the combination of the references does not provide the teachings necessary to successfully obtain the presently claimed invention. Nonetheless, in the interests of furthering the prosecution of this application, yet without acquiescing to the Examiner's arguments or waiving any arguments pertaining to the impropriety of combining these references, these references are discussed on their merits.

As discussed above, Au-Young does not teach the TL-γ of the presently claimed invention nor modulators of this protein. The Foulkes *et al.* reference teaches methods to identify compounds useful in the treatment of cardiovascular disease. There is no teaching in Foulkes *et al.* of screening methods to detect modulators of TL-γ. Thus, there is no teaching in either cited reference of TL-γ, as recited in the presently pending Claims. Thus, even if these references are combined, the present invention is not the result. Rather, the combination of these references might lead one to produce methods to screen for PAC10 proteins that are associated with cardiovascular disease, or perhaps, methods to identify modulators of PAC10 proteins that would ameliorate cardiovascular disease.

Applicants also submit that the Examiner must take the references *as a whole* into consideration (the critical inquiry is whether "'there is something in the prior art as a whole *to suggest* the desirability, and thus the obviousness, of making the combination.' "*Fromson v. Advance Offset Plate, Inc.*, 755 F.2d 1549, 1556, 225 USPQ 26 (Fed. Cir. 1985) (emphasis in the original), quoting *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co., 730 F.2d 1452, 1462*, 221 USPQ 481,488 (Fed. Cir. 1984)). Furthermore, "[i]t is impermissible, within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art." *In re Wesslau*, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965), cited in *In re Hedges*, 228 USPQ 685, 687 (Fed. Cir. 1986)).

Applicants further submit that there is simply no guidance provided in either of these cited references of methods to screen for modulators of TL-γ, as presently claimed. Even by

improperly picking and choosing a general protocol for high-throughput assays, as discussed by Foulkes *et al.*, the Examiner has not provided evidence that the teachings of Foulkes *et al.* and/or Au-Young *et al.* would lead one of skill in the art to the presently claimed invention.

As the combination of the teachings in the references do not result in the presently claimed invention, Applicants assert that by suggesting that the cited art may be used to produce the methods of the presently claimed invention, the Examiner presents, in essence, an "obvious to experiment" or "obvious to try" standard for obviousness. The "obvious to try" standard has been thoroughly discredited. Indeed, an obviousness rejection is inappropriate, where the prior art [gives] either no indication of which parameters [are] critical or no direction as to which of many possible choices is likely to be successful" (quoting *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 [Fed. Cir. 1988], *Merck & Co., Inc. v. Biocraft Laboratories, Inc.*, 10 USPQ2d 1843, 1845 [Fed. Cir. 1989]). There is no teaching in either of the cited references regarding methods to screen for modulators of TL-γ. Thus, there is simply nothing in the cited prior art that would provide one of ordinary skill in the art with the knowledge necessary to develop such screening methods (*i.e.*, with the parameters and elements necessary to successfully conduct the presently claimed methods).

In sum, Applicants submit that the newly added Claims are unobvious over Au-Young *et al.* and Foulkes *et al.*, taken either alone or in combination. Thus, Applicants respectfully request that this rejection be withdrawn.

B. The Claims are Unobvious Over Au-Young

In regards to Au-Young and Claims 34-39, 41, and 43-46, the Examiner argues that it would have been obvious to "assemble together in a kit all the reagents and instructions required to perform the method because kits provide convenience and economy to the consumer and the assembly of screen-assay reagents in kit format is routine in the art." Applicants must respectfully disagree.

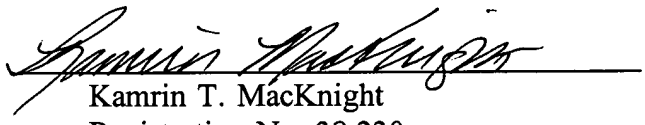
Applicants respectfully submit that the kit embodiments of newly added Claims 70-74 are unobvious over Au-Young, as Au-Young does *not* teach methods to screen for TL-γ modulators. The fact that Applicants have provided a particular "kit" format for their novel and unobvious invention is of no moment. Indeed, "routine experimentation" or something that is "routine in the art" does not negate patentability. (*See, in re Fay*, 347 F.2d 597, 146 USPQ 47, 51 (CCPA 1965); 35 U.S.C. § 103(a) ["Patentability shall not be negatived by the

manner in which the invention was made"]). Thus, even if "routine experimentation" would lead one of ordinary skill in the art to produce the kit embodiments of the presently claimed invention, (something the Applicants vigorously contest, as there is nothing in the cited prior art that teaches the methods of the presently claimed invention), the Examiner's statement that "the assembly of screen-assay reagents in kit format is routine in the art" (Office Action, page 7), is an improper basis for rejection. Indeed, as the methods provided in the kit are not obvious, the configuration of these methods in a kit format is likewise unobvious. Thus, Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that Applicant's Claims as amended should be passed to allowance. If a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect at (415) 705-8410.

Dated: January 31, 2001



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